Emerging respiratory infections: MERS and beyond

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### Emerging Infections

- **What are emerging infections?**
  - New infection
  - Known infection: rapid increase in incidence or widened geographical range

- Of 335 emerging infections between 1940-2004, 60% were zoonosis (72% from wildlife).
  - **Organism:**
    - 54% bacteria or rickettsia
    - 25% viruses

- **Table 1: Emerging respiratory viruses**
  - SARS=severe acute respiratory syndrome. MERS=Middle East respiratory syndrome.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Year</th>
<th>Region</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hantavirus pulmonary syndrome, sin nombre virus</td>
<td>1993</td>
<td>USA</td>
</tr>
<tr>
<td>Influenza A H5N1</td>
<td>1997</td>
<td>Hong Kong</td>
</tr>
<tr>
<td>Influenza A H9N2</td>
<td>1999</td>
<td>Hong Kong</td>
</tr>
<tr>
<td>Human metapneumovirus</td>
<td>2001</td>
<td>Netherlands</td>
</tr>
<tr>
<td>SARS coronavirus</td>
<td>2003</td>
<td>Hong Kong</td>
</tr>
<tr>
<td>Human coronavirus NL63</td>
<td>2004</td>
<td>Netherlands</td>
</tr>
<tr>
<td>Influenza A H7N7</td>
<td>2004</td>
<td>Netherlands</td>
</tr>
<tr>
<td>Human coronavirus HKU1</td>
<td>2005</td>
<td>China</td>
</tr>
<tr>
<td>Influenza A, H1 triple reassortant</td>
<td>2005</td>
<td>USA</td>
</tr>
<tr>
<td>Triple reassortant H3N2 influenza A viruses</td>
<td>2005</td>
<td>Canada</td>
</tr>
<tr>
<td>Bocavirus</td>
<td>2005</td>
<td>Sweden</td>
</tr>
<tr>
<td>Influenza A H1N1 pdm09</td>
<td>2009</td>
<td>Mexico</td>
</tr>
<tr>
<td>Adenovirus 14</td>
<td>2010</td>
<td>USA</td>
</tr>
<tr>
<td><strong>MERS-coronavirus</strong></td>
<td>2012</td>
<td>Saudi Arabia</td>
</tr>
<tr>
<td>Influenza A H7N9</td>
<td>2013</td>
<td>China</td>
</tr>
</tbody>
</table>
68 year old man

- 4 day history of fever, dry cough and sore throat
- 24 hours increasing shortness of breath
- PMH: diabetes, non-smoker

**O/E:**
- Temperature 39
- HR 110, BP 130/50
- GCS 15/15
- RR 26, Sats 82% (air), crackles right mid-zone

**Ix:** wcc: 0.9 (lymphopaenia), platelets: 110
CXR

• Pneumonia
• Aetiology?

Assiri et al Lancet ID 2013
Additional clues?

- Sick contacts
- Exposure to air conditioning
- Travel history

- Patients don’t always volunteer a travel history
- Doctors don’t ask
  – post-travel risk assessment is recorded in 5-20% of potentially eligible patients presenting to hospital in UK\(^1,2,3\)

\(^1\)Smith 2005, \(^2\)Price 2011, \(^3\)Anthalee J Infec 2007
CAP and travel

**Americas**
- Endemic fungi

**Middle East**
- MERS-CoV

**Asia**
- Avian Influenza
- Melioidosis

**Global:**
- *Rural farming areas*
  - *Coxiella burnetii*
- *Air conditioning*
  - *Legionella sp.*
- **Southern hemisphere (winter)**
  - Seasonal Influenza
The vital clue......

“My son has just been admitted to intensive care with a chest infection”

“He’s just got back from Saudi Arabia”
MERS CO-V
What is MERS?

• **Middle East Respiratory Syndrome**

• Novel coronavirus

• First identified in Jeddah, Saudi Arabia in 2012

• Ongoing outbreak in Middle East
Confirmed global cases of MERS-CoV

Reported to WHO as of 30 Dec 2015 (n=1625)

Republic of Korea:
186 cases
36 deaths
16693 monitored for 14 days

UK:
2012, 1 case
2013, 3 cases

Total: 1625 cases, 586 deaths (7/1/16)
Where has MERS-CoV come from?

• Identical (or near identical) virus has been isolated from geographically linked humans and camels\(^1\)

• High prevalence of MERS-CoV Ab in
  – camels (not in cows, goats, sheep)\(^2\)
  – camel shepherds and slaughterhouse workers v general pop\(^3\)

\(^1\)Azhar NEJM 2014; \(^2\)Meyer EID 2014, Hemida Euro Surveill 2013, Reusken Euro Surveill 2013; \(^3\)Muller LancetID 2015
Case-control study

- 30 primary cases (116 neighbourhood controls)
- direct contact* with dromedary in 2 weeks prior to symptom onset (adjusted OR 7.45, 95% CI 1.57–35.28)

* Physical contact with animals or animal products in any setting
Human infections

Saudi Arabia: 1275 lab-confirmed cases (2012-4/11/15)¹

<table>
<thead>
<tr>
<th>Source of Infection</th>
<th>Proportion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
<td>38%</td>
</tr>
</tbody>
</table>

¹Saudi Arabia MOH
Human infections

NOT seeing sustained transmission
R0 < 1

Adapted from virologydownunderblogpost.com.au
### Clinical Presentation

- **Fever**
- **Chills**
- **Cough**
- **SOB**

**Incubation Period:**
- 5 days (2 - 13 days)

### Symptoms in Patients (n=47)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Patients (n=47)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>46 (98%)</td>
</tr>
<tr>
<td>Fever with chills or rigors</td>
<td>41 (87%)</td>
</tr>
<tr>
<td>Cough</td>
<td>39 (83%)</td>
</tr>
<tr>
<td>Dry</td>
<td>22 (47%)</td>
</tr>
<tr>
<td>Productive (sputum)</td>
<td>17 (36%)</td>
</tr>
<tr>
<td>Haemoptysis</td>
<td>8 (17%)</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>34 (72%)</td>
</tr>
<tr>
<td>Chest pain</td>
<td>7 (15%)</td>
</tr>
<tr>
<td>Sore throat</td>
<td>10 (21%)</td>
</tr>
<tr>
<td>Runny nose</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>8 (17%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>10 (21%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>10 (21%)</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>12 (26%)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>15 (32%)</td>
</tr>
<tr>
<td>Headache</td>
<td>6 (13%)</td>
</tr>
</tbody>
</table>

Zumla Lancet 2015; Assiri et al Lancet ID 2013
Investigations

<table>
<thead>
<tr>
<th>Laboratory results</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest radiography abnormalities</td>
<td>100%</td>
</tr>
<tr>
<td>Leucopenia ($&lt;4\cdot0 \times 10^9$ cells per L)</td>
<td>14%</td>
</tr>
<tr>
<td>Lymphopenia ($&lt;1\cdot5 \times 10^9$ cells per L)</td>
<td>34%</td>
</tr>
<tr>
<td>Thrombocytopenia ($&lt;140 \times 10^9$ cells per L)</td>
<td>36%</td>
</tr>
<tr>
<td>Increased amount of lactate dehydrogenase</td>
<td>49%</td>
</tr>
<tr>
<td>Increased amount of alanine aminotransferase</td>
<td>11%</td>
</tr>
<tr>
<td>Increased amount of aspartate aminotransferase</td>
<td>15%</td>
</tr>
</tbody>
</table>

Assiri Lancet 2013
Clinical Spectrum

Risk Factors for severe infection

- Immunocompromised
- Co-morbidities
- Smoking
- Concomitant infection
- Low albumin
- Age >65 (mortality)

CFR: 40%
Returning from the Middle East?

Important information about Middle East Respiratory Syndrome (MERS)

A new disease called MERS has been identified in some countries in the Middle East.

The risk to most travellers is very low, but we advise returning travellers:

- to be aware of the symptoms of MERS
- the symptoms include fever and cough, or shortness of breath
- if you become unwell with these symptoms within 14 days of being in the Middle East, call your doctor and tell them where you have travelled

For more information visit: www.gov.uk/phe

For health advice, call NHS 111
UK guidance: who to test?

• Acute respiratory infection requiring hospital admission
  – Fever, cough + lung parenchymal disease
  – Unknown aetiology

• Plus one of
  – Travel to MERS-endemic country* within 14 days of symptom onset
  – Contact with symptomatic confirmed case within 14 days of symptom onset

*Bahrain, Jordan, Iraq, Iran, Kingdom of Saudi Arabia, Kuwait, Oman, Qatar, United Arab Emirates, Yemen
UK guidance: who to test?

• Acute respiratory infection requiring hospital admission
  – Fever, cough + lung parenchymal disease
  – Unknown aetiology

• Plus one of:
  – ICU HCW caring for patient with severe acute respiratory infection
  – Cluster (2+) of epidemiologically linked cases within a 2 week period requiring ICU admission
UK guidance: testing

• **What samples?**
  – Sputum (or BAL)
  – Throat & nose swab in viral transport medium x 2
  – Acute serum sample

• **Handling of samples**
  – Double bag + biohazard sticker
  – Containment level 3
  – Category B transport

• **How do I request?**
  – Call local ID/micro → call local PHE → Arrange transport to MERS-testing labs
UK guidance: infection control

• **Isolation:**
  – Triage: single room
  – Admission: negative pressure single room

• **PPE:**
  – long sleeved fluid repellent gown, surgical gloves, FFP3 mask, eye protection

• **Staff:**
  – Inform infection control
  – Restricted entry / log book
  – Self-monitor for 14 days and report if fever
Travellers: infection control

Consult a health worker if you have fever, cough or difficulty breathing. Isolate them from others while you wait for their test results.

Wash your hands regularly with soap and water and maintain good personal hygiene.

Avoid close contact with anyone with a fever, cough or difficulty breathing.

Cover your mouth and nose with a tissue or your sleeve when coughing or sneezing.

World Health Organization

MERS-CoV
Middle East respiratory syndrome coronavirus

X
AND BEYOND.....
Avian Influenza

• H5N1: 846 lab-confirmed cases, 449 deaths
• H5N6: 10 cases
• H7N9: Current outbreak in China, 693 lab-confirmed cases, 277 deaths

WHO
Enterovirus D68

Picornavirus, first isolated 1962

- Sporadic cases identified, 1970-2005
- Small clusters in US, Asia, Europe 2005-2010
- Worldwide emergence 2010-2014

- Biologically similar to rhinovirus
- Epidemiology not fully understood
  - Predominantly children, however also described in adults
- Clinically
  - Severe respiratory disease
  - Possible association with acute flaccid paralysis

2014: confirmed cases in USA N=1153

Messacar J Med Vir 2015
Emerging infections: summary

• Appears to be an increase in emerging infections over time

• Major public health concern and potential threat to global security

• HCW are on the front-line
  – Awareness
  – Travel history
  – Infection control
Clinical advice

Fever service:
08447788990

HTD national advice line:
02034567890
(ask for HTD on-call)
Antimicrobial resistance

*S. pneumoniae*

Macrolide resistance

- UK 5.1%
- Cyprus 0%
- Romania 46.7%

Penicillin resistance
Key lessons

- Increase in frequency and spectrum of antibiotic resistance

- Geographical variation:
  - Asia / Mediterranean >>> UK

- What should you do?
  - Take a travel history!!!!
  - Follow antibiotic guidelines
  - Discuss with ID / Micro if travelled*

* Other risk factors: recurrent UTIs, treatment failure, prior known resistant isolates, care home resident recent hospitalisation (Ben-Ami CID 2009; Jain JAC 2014)